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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/868,196	08/02/2001	Irma H. Russo	13254-00012	6024

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EXAMINER	
YU, MISOOK	
ART UNIT	PAPER NUMBER
1642	

DATE MAILED: 04/09/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/868,196	RUSSO ET AL.	
	Examiner	Art Unit	
	MISOOK YU, Ph.D.	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *09 January 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *45,55-65,70-78 and 80* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *45, 55-65, 70-78, and 80* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Claims 45, 55-65, 70-78, and 80 are pending and are under consideration.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office Action.

This Office action contains new grounds of rejection.

Claim Rejections - 35 USC § 102

Claims 45, 55-58, 70, and 75 remain rejected for reason of record under 35 U.S.C. **102(b)** as being anticipated by any one of Srivastava et al (1997, IDS AX, cited in ISR, Carcinogenesis, vol. 18, pages 1799-1808), Russo et al (1990, IDS AS, J. Natl, Cancer Inst. Vol. 82, pages 1286-1287), or Russo et al (1990, IDS AT, Br. J. Cancer, vol. 62, pages 2343-7).

Claim 45 (the base claim of the claimed invention) is interpreted as drawn to method of treating or preventing mammary tumors with an active step of administering an effective amount of hCG to a host that needs prevention of clinically manifest mammary tumor, claim 55 further limits the tumor to be a primary tumor, claim 56 further limits the tumor to be a non-invasive carcinoma, claim 57 further limits the carcinoma to be a in situ or lobular carcinoma in situ, claim 58 further limits the tumor to be invasive carcinoma, claim 70 further limits the amount to be 100 to 20,000 IU per day, and claim 75 further limits hCG to be administered for several weeks.

Applicant argues that none of the cited references a method of treating or preventing clinically manifest mammary tumors by administering hCG to a host having a clinically manifest mammary tumor; in no instant does any of the reference disclose that

tumors were clinically manifest in the rats at the initiation of hCG treatment; Rosso et al specifically disclose that animals did not begin developing palpable tumors until six weeks after DMBA injection; and Stinvastava et al report that the earliest finding of a mammary tumor following DMBA administration was at 70 days of age. This argument has been fully considered but found unpersuasive for several reasons:

First, the argument with Stinvastava et al report that the earliest finding of a mammary tumor following DMBA administration was at 70 days of age is not persuasive because Srivastava et al at Fig. 1 teach that hCG was given to mice from 25 days to105 days after DMBA administration (look at the Fig. 1, DMBA +hCG line) well after the finding of mammary tumor according to applicant's argument, thus the hCG was administered in Stinvastava et al to a host having clinically manifest mammary tumor from day 95 to 105. Srivastava et al teach method of treating/preventing DMBA-induced mammary tumor (non invasive, invasive, carcinoma) by administering 100 IU hCG obtained from Sigma to a host for 40 days. Note Figs. 1 and 2, and Table I and II at page 1801.

Second, the rejection of record also stands because the Office is completely confused about applicant's argument in light of the purpose set out in the preamble of the base claim 45 i.e. "preventing clinically manifest mammary tumors". What is being prevented if a host already has a clinically manifest mammary tumor? It appears that prevention of a condition that has already transpired is logically impossible. See the rejections under 35 U.S.C. 112 below for further explanation.

Claims 45, 58, 60-64, and 70-72 remain rejected for reason of record under 35 U.S.C. **102(b)** as being anticipated by Grattarola (1976, Journal of the National Cancer Institute, vol. 56, pages 11-16).

Claim 45 (the base claim of the claimed invention) is interpreted as drawn to method of treating or preventing mammary tumors with an active step of administering an effective amount of hCG to a host that needs prevention or treatment of clinically manifest mammary tumor, wherein claim 58, and 60 further limit the mammary tumor to be invasive, and metastatic tumors respectively, claim 61 and 62 further limit the host to be pre-menopausal or post-menopausal woman, claims 63 and 64 further limit the therapy to be combined with other therapy, surgery or chemotherapy respectively, claims 70-72 further limits amount of hCG.

Applicant argues that Grattarola no where discloses a method of treating or preventing clinically manifest mammary tumors by administering hCG to a host having clinically manifest mammary tumor; Grattarola was not a treatment of mammary tumors; Grattarola was to post-mastectomy, post-ovariectomy patients, who, by definition, could not have had a clinically manifest mammary tumor at the time because those tumors had been removed previously by surgery; and Grattarola no where teaches or discloses the use of hCG to treat mammary tumors whether clinically manifest or not. These arguments have been fully considered but found unpersuasive for the following reasons.

As for the argument that Grattarola no where teaches or discloses the use of hCG to treat mammary tumors whether clinically manifest or not, the Office treats the preamble of the instant base claim as non-limiting, since the language does not result in

manipulative difference in steps of claims. It is the Office's position that the instantly claimed breast treatment/prevention method is anticipated by Grattarola, who teaches the active step of instant method with the same amount of the active ingredient, i.e. method of administering 15,000 IU hCG to advanced breast cancer patients who are either pre-menopausal and post-menopausal, and had undergone surgery. Note abstract, page 11-12, Table 1. Note the amount used in the prior art is the same amount used in instant claims 70-72. Therefore, the method taught by Grattarola would inherently result in the purpose stated in the preamble of instant claim, thus anticipating instant claims. See Bristol-Myers Squibb Co. v. Ben Venue Laboratories Inc., 58 USPQ2d 1508 (CA FC 2001).

As for the argument about a host clinically manifest mammary tumor, see 102 (b) art rejection above. The currently amended base claim as construed is confusing as to what is being prevented. Therefore the argument about a host clinically manifest mammary tumor is not persuasive. Further, applicant's argument that instantly drawn treatment method is giving hCG to a host with clinically manifest (see instant claim 45) and metastatic mammary tumor (see instant claim 60) and the art teaches giving hCG to a patient who had undergone surgery is persuasive either because who in the world would do not want to have surgery until mammary tumor being metastasized so that they can receive hCG, and then have surgery. Note the instant claim 64 which says surgery. The specification as originally filed did not say instant invention is to give hCG to a breast cancer patient first before surgery even if the primary tumor is likely to be

metastasized. For all above reasons, Grattarola anticipates instant claims 45, 58, 60-64, and 70-72.

Claim 45, 70-72, and 77 are rejected under 35 U.S.C. **102(b)** as being anticipated by Saal et al, Fertil Steril. 1991 Aug;56(2):225-9 as evidenced by Russo et al (cited above, 1990, IDS AT).

Claim 45 (the base claim of the claimed invention) is interpreted as drawn to method of treating or preventing mammary tumors with an active step of administering an effective amount of hCG to a host that needs prevention of clinically manifest mammary tumor to with the recited amounts (claims 70-72) of hCG subcutaneously (claim 77).

Applicant argues that since the now cancelled claim 54 was not rejected, and the limitation "clinically manifest mammary tumor" was incorporated into the base claim, this rejection should be withdrawn. This argument has been fully considered but found unpersuasive. As stated in the two 102 (b) art rejections above, the claims are interpreted as drawn to method of treating or preventing mammary tumors with an active step of administering an effective amount of hCG to a host that needs prevention of clinically manifest mammary tumor to a host because prevention of a condition that already transpired seems seemingly illogical. Therefore, this rejection still stands until this issue is resolved.

Claim 45, and 70-77 are rejected under 35 U.S.C. **102(b)** as being anticipated by Anapliotou et al, Fertil Steril. 1996 Aug;66(2):305-11, as evidenced by Russo et al (cited above, 1990, IDS AT).

Claim 45 (the base claim of the claimed invention) is interpreted as drawn to method of treating or preventing mammary tumors with an active step of administering an effective amount of hCG to a host that needs prevention of clinically manifest mammary tumor with the recited amounts in claims 70-72 of hCG with the recited schedule, duration, and route recited in claims 73-76.

Applicant argues that since the now cancelled claim 54 was not rejected, and the limitation "clinically manifest mammary tumor" was incorporated into the base claim, this rejection should be withdrawn. This argument has been fully considered but found unpersuasive. As stated in the two 102 (b) art rejections above, the claims are interpreted as drawn to method of treating or preventing mammary tumors with an active step of administering an effective amount of hCG to a host that needs prevention of clinically manifest mammary tumor to a host because prevention of a condition that already transpired seems seemingly illogical. Therefore, this rejection still stands until this issue is resolved.

Claim Rejections - 35 USC § 103

Claim 59 remains rejected for reason of record under 35 U.S.C. 103(a) as being unpatentable over any one of Srivastava et al (1997, IDS AX, cited in ISR, Carcinogenesis, vol. 18, pages 1799-1808), Russo et al (1990, IDS AS, J. Natl, Cancer

Inst. Vol. 82, pages 1286-1287), or Russo et al (1990, IDS AT, Br. J. Cancer, vol. 62, pages 2343-7) as applied to claims 45 and 58 above, and further in view of Silverstein et al (1994, Cancer, vol. 73, pages 1673-7, abstract only).

Claim 59 is interpreted as drawn to method of treating mammary tumors with an active step of administering an effective amount of hCG to patient with tubular or lobular invasive carcinoma as clinically manifest mammary tumor.

Applicant argues that there is no motivation and none of Srivastava et al Russo et al, or Russo et al teaches giving hCG to a host having clinically manifest mammary tumor. This argument has been fully considered but found unpersuasive because Srivastava et al for example, teach giving hCG to a host having clinically manifest mammary tumor. See the 102(b) art rejection above for further detail; "hCG treatment a useful approach for the prevention and therapy of breast cancer" in the last line of the abstract by Srivastava et al, for example.

Claim 65 is rejected under 35 U.S.C. 103(a) as being unpatentable over any one of Srivastava et al (1997, IDS AX, cited in ISR, Carcinogenesis, vol. 18, pages 1799-1808), Russo et al (1990, IDS AS, J. Natl, Cancer Inst. Vol. 82, pages 1286-1287), or Russo et al (1990, IDS AT, Br. J. Cancer, vol. 62, pages 2343-7) as applied to claim 45 above, and further in view of Mgbonyebi et al (1997, IDS AL).

The claim is drawn to method of administering the active ingredient to estrogen positive mammary tumor.

Applicant argues that there is no motivation and none of Srivastava et al Russo et al, or Russo et al teaches giving hCG to a host having clinically manifest mammary tumor. This argument has been fully considered but found unpersuasive because Srivastava et al for example, teach giving hCG to a host having clinically manifest mammary tumor. See the 102(b) art rejection above for further detail; "hCG treatment a useful approach for the prevention and therapy of breast cancer" in the last line of the abstract by Srivastava et al, for example.

Mgbonyebi et al (1997, IDS AL) teach hCG is effective in inhibition of estrogen positive breast cancer cells, Therefore, it would have been obvious to one having ordinary skill in the art at the time the claimed invention was made to detect which breast cancer is estrogen positive and practice instantly claimed invention with reasonable expectation of success.

Claim 78 is rejected under 35 U.S.C. 103(a) as being unpatentable over any one of Srivastava et al (1997, IDS AX, cited in ISR, Carcinogenesis, vol. 18, pages 1799-1808), Russo et al (1990, IDS AS, J. Natl, Cancer Inst. Vol. 82, pages 1286-1287), or Russo et al (1990, IDS AT, Br. J. Cancer, vol. 62, pages 2343-7) as applied to claim 45 above, and further in view of any one of Platanias et al (J Biol Chem. 1998 Mar 6;273:5577-81), Oberg et al (1989, J Natl Cancer Inst., vol. 81, pages 531-5), Recchia et al (Clin Ter. 1998 May-Jun;149:203-8), or Robinson et al (1990, Breast Cancer Res. Treat., vol. 15, pages 95-101, abstract only)

The claim is interpreted as drawn to a method of administering Type I interferon in combination with hCG.

Applicant argues that there is no motivation and none of Srivastava et al Russo et al, or Russo et al teaches giving hCG to a host having clinically manifest mammary tumor. This argument has been fully considered but found unpersuasive because Srivastava et al for example, teach giving hCG to a host having clinically manifest mammary tumor. See the 102(b) art rejection above for further detail; "hCG treatment a useful approach for the prevention and therapy of breast cancer" in the last line of the abstract by Srivastava et al, for example.

Any of the references teaches that Type I interferon has anti-tumor activity, Therefore, it would have been obvious to one having ordinary skill in the art at the time the claimed invention was made to use Type I interferon known to have anti-tumor effect with reasonable expectation of success.

Claim 80 is rejected under 35 U.S.C. 103(a) as being unpatentable over any one of Srivastava et al (1997, IDS AX, cited in ISR, Carcinogenesis, vol. 18, pages 1799-1808), Russo et al (1990, IDS AS, J. Natl, Cancer Inst. Vol. 82, pages 1286-1287), or Russo et al (1990, IDS AT, Br. J. Cancer, vol. 62, pages 2343-7) as applied to claim 45 above, and further in view of Sigma catalog (1995, page 263 only).

The claim is drawn to the method using recombinant hCG.

Applicant argues that there is no motivation and none of Srivastava et al Russo et al, or Russo et al teaches giving hCG to a host having clinically manifest mammary

tumor. This argument has been fully considered but found unpersuasive because Srivastava et al for example, teach giving hCG to a host having clinically manifest mammary tumor. See the 102(b) art rejection above for further detail; "hCG treatment a useful approach for the prevention and therapy of breast cancer" in the last line of the abstract by Srivastava et al, for example.

The Sigma catalog says that the recombinant hCG is commercially available, therefore it is the Office's position that claim 80 is an obvious variation of the base claim and one in ordinary skill would have practiced the instantly claimed invention with reasonable expectation of success before the effective filing date of instant invention.

The Following Are New Grounds of Rejection

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 45, 55-65, 70-78, and 80 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The newly amended base claim 45 and applicant's argument traversing the art rejection above say that the invention is drawn to treating or preventing clinically manifest mammary tumors by giving hCG to a host having a clinically manifest mammary tumor. The newly amended base claim excludes a host that has not yet developed a mammary tumor before giving hCG. It is not clear how what is the metes

and bounds of the limitation "prevent". What is being prevented if a host already has clinically manifest mammary tumor? It appears that prevention of a condition that has already transpired is logically impossible. However, the Office does not contest that such prevention method exists. Applicant is kindly requested to provide the Office some education on this matter.

Claims 45, and 60 are confusing in light of applicant argument traversing the art rejection of record. Do claims 45, 60 mean that hCG is given patient who does not like to have surgery and who waits mammary tumor to be metastastic or who did not know they had mammary tumor until it had metastasized?

Claims 45, 64, and 65 are also confusing in light of applicant's argument traversing the art rejection in terms of what "combined" means. Does it mean other cancer therapy such as surgery is given to a host with clinically manifest mammary tumor only after hCG treatment is initiated?

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 45, 55-65, 70-78, and 80 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is new matter

rejection. This rejection is made because the newly amended claims 45, 55-65, 70-78, and 80 are interpreted as drawn method of preventing clinically manifest mammary tumors by giving hCG to a host having a clinically manifest mammary tumor. The specification at page 32-33 teaches that method of preventing clinically manifest mammary tumors by giving hCG to a host that does not have clinically manifest mammary tumors. Applicant is kindly requested to point out the support in the specification as originally filed for method of preventing clinically manifest mammary tumors by giving hCG to a host having a clinically manifest mammary tumor, since the support is not apparent to the Office.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of

the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to MISOOK YU, Ph.D. whose telephone number is 571-272-0839. The examiner can normally be reached on 8 A.M. to 5:30 P.M., every other Friday off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne C Eyler can be reached on 571-272-0871. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

MISOOK YU, Ph.D.
Examiner
Art Unit 1642

LARRY R. HELMS, PH.D
PRIMARY EXAMINER